

CLAIMS

What is claimed is:

1. An isolated nucleic acid fragment encoding an aspartyl-tRNA synthetase comprising a member selected from the group consisting of:

5 (a) an isolated nucleic acid fragment encoding an amino acid sequence that is at least 80% identical to the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:2, 4, 6 and 8;

(b) an isolated nucleic acid fragment that is complementary to (a).

10 2. The isolated nucleic acid fragment of Claim 1 wherein nucleic acid fragment is a functional RNA.

3. The isolated nucleic acid fragment of Claim 1 wherein the nucleotide sequence of the fragment comprises the sequence set forth in a member selected from the group consisting of SEQ ID NO:1, 3, 5 and 7.

15 4. A chimeric gene comprising the nucleic acid fragment of Claim 1 operably linked to suitable regulatory sequences.

5. A transformed host cell comprising the chimeric gene of Claim 4.

6. An aspartyl-tRNA synthetase polypeptide comprising all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:2, 4, 6 and 8

20 7. An isolated nucleic acid fragment encoding a cysteinyl-tRNA synthetase comprising a member selected from the group consisting of:

(a) an isolated nucleic acid fragment encoding an amino acid sequence that is at least 80% identical to the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:10, 12 and 14;

(b) an isolated nucleic acid fragment that is complementary to (a).

8. The isolated nucleic acid fragment of Claim 7 wherein nucleic acid fragment is a functional RNA.

30 9. The isolated nucleic acid fragment of Claim 7 wherein the nucleotide sequence of the fragment comprises the sequence set forth in a member selected from the group consisting of SEQ ID NO:9, 11 and 13.

10. A chimeric gene comprising the nucleic acid fragment of Claim 7 operably linked to suitable regulatory sequences.

35 11. A transformed host cell comprising the chimeric gene of Claim 10.

12. A cysteinyl-tRNA synthetase polypeptide comprising all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:10, 12 and 14.

13. An isolated nucleic acid fragment encoding a tryptophanyl-tRNA synthetase comprising a member selected from the group consisting of:

- (a) an isolated nucleic acid fragment encoding an amino acid sequence that is at least 80% identical to the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:16, 18 and 20;
- (b) an isolated nucleic acid fragment that is complementary to (a).

14. The isolated nucleic acid fragment of Claim 13 wherein nucleic acid fragment is a functional RNA.

15. The isolated nucleic acid fragment of Claim 13 wherein the nucleotide sequence of the fragment comprises the sequence set forth in a member selected from the group consisting of SEQ ID NO:15, 17 and 19.

16. A chimeric gene comprising the nucleic acid fragment of Claim 13 operably linked to suitable regulatory sequences.

17. A transformed host cell comprising the chimeric gene of Claim 16.

18. A tryptophanyl-tRNA synthetase polypeptide comprising all or a substantial portion of the amino acid sequence set forth in a member selected from the group consisting of SEQ ID NO:16, 18 and 20.

19. An isolated nucleic acid fragment encoding a tyrosyl-tRNA synthetase comprising a member selected from the group consisting of:

- (a) an isolated nucleic acid fragment encoding an amino acid sequence that is at least 80% identical to the amino acid sequence set forth in SEQ ID NO:22;
- (b) an isolated nucleic acid fragment that is complementary to (a).

20. The isolated nucleic acid fragment of Claim 19 wherein nucleic acid fragment is a functional RNA.

21. The isolated nucleic acid fragment of Claim 19 wherein the nucleotide sequence of the fragment comprises the sequence set forth in SEQ ID NO:21.

22. A chimeric gene comprising the nucleic acid fragment of Claim 19 operably linked to suitable regulatory sequences.

23. A transformed host cell comprising the chimeric gene of Claim 22.

24. A tyrosyl-tRNA synthetase polypeptide comprising all or a substantial portion of the amino acid sequence set forth in SEQ ID NO:22.

25. A method of altering the level of expression of an aminoacyl-tRNA synthetase in a host cell comprising:

- (a) transforming a host cell with the chimeric gene of any of Claims 4, 10, 16 and 22; and

(b) growing the transformed host cell produced in step (a) under conditions that are suitable for expression of the chimeric gene wherein expression of the chimeric gene results in production of altered levels of an aminoacyl-tRNA synthetase in the transformed host cell.

5 26. A method of obtaining a nucleic acid fragment encoding all or a substantial portion of the amino acid sequence encoding an aminoacyl-tRNA synthetase comprising:

- (a) probing a cDNA or genomic library with the nucleic acid fragment of any of Claims 1, 7, 13 and 19;
- (b) identifying a DNA clone that hybridizes with the nucleic acid fragment
- 10 of any of Claims 1, 7, 13 and 19;
- (c) isolating the DNA clone identified in step (b); and
- (d) sequencing the cDNA or genomic fragment that comprises the clone isolated in step (c)

wherein the sequenced nucleic acid fragment encodes all or a substantial portion of the amino acid sequence encoding an aminoacyl-tRNA synthetase.

15 27. A method of obtaining a nucleic acid fragment encoding a substantial portion of an amino acid sequence encoding an aminoacyl-tRNA synthetase comprising:

- (a) synthesizing an oligonucleotide primer corresponding to a portion of the sequence set forth in any of SEQ ID NOs:1, 3, 5, 7, 9, 11, 13, 15,
- 20 17, 19 and 21; and
- (b) amplifying a cDNA insert present in a cloning vector using the oligonucleotide primer of step (a) and a primer representing sequences of the cloning vector

wherein the amplified nucleic acid fragment encodes a substantial portion of an amino acid sequence encoding an aminoacyl-tRNA synthetase.

25 28. The product of the method of Claim 26.

29. The product of the method of Claim 27.

30. A method for evaluating at least one compound for its ability to inhibit the activity of an aminoacyl-tRNA synthetase, the method comprising the steps of:

- (a) transforming a host cell with a chimeric gene comprising a nucleic acid fragment encoding an aminoacyl-tRNA synthetase, operably linked to suitable regulatory sequences;
- (b) growing the transformed host cell under conditions that are suitable for expression of the chimeric gene wherein expression of the chimeric gene results in production of the aminoacyl-tRNA synthetase encoded by the operably linked nucleic acid fragment in the transformed host cell;
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- (c) optionally purifying the aminoacyl-tRNA synthetase expressed by the transformed host cell;
 - (d) treating the aminoacyl-tRNA synthetase with a compound to be tested; and
 - (e) comparing the activity of the aminoacyl-tRNA synthetase that has been treated with a test compound to the activity of an untreated aminoacyl-tRNA synthetase,
- thereby selecting compounds with potential for inhibitory activity.